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An Apparatus for Concentrating and or Purifying Macromolecules in a Solution and a Method for Manufacturing such an Apparatus

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Description

This invention concerns an apparatus for the concentration and/or purification of macro molecules in a solution and also concerns a procedure for the manufacturing of such an apparatus. The apparatus incorporates a chamber (or compartment) for the sample to be treated and a chamber for the filtrate which is to be separated by means of at least one membrane. Expressed more exactly, the invention concerns a new type of fastening of a membrane in a pressure resistant, sealing manner on border surfaces between the two chambers. Apparatuses, which are made in accordance with the invention, can be used in centrifuges, as tangential flow modules, as gas pressure cells or as hand operated spraying apparatuses.

Many biotechnical laboratories and institutions related to health care employ microfiltration and ultrafiltration for the treatment of biological solutions. For example, filtration is used as a step in sterilization for the removal of bacteria, as a clarification means for the removal of suspended solids and contaminating material. Filtration is also used as a concentration step for proteins and other macromolecules or again as a purification step for the elimination of undesired micromolecules such as salts. Alternative filtration processes, apparatuses and isolation by membranes are used, where appropriate, in certain applications and process requirements.

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Centrifugal forces, gas or liquid pressure or vacuum are typically put to use in order to create the vector or gradient necessary to press or pull solvent and small micromolecules through a membrane while solution components, which are greater than the exclusion limit of the membrane are held back. In the case of the most frequent applications, the speed of filtration in relation to the employed membrane surface is just so

much greater, the greater is the applied pressure or vacuum In general, apparatuses with small surface and a high filtering speed are preferred.

Typical apparatuses of the type of spoken of here include in their construction a chamber for the sample to be treated, and a chamber for the filtrate. These chambers are connected by at least one common opening, in which a porous membrane may be placed, this being such a membrane as is suitable for microporous or ultrafiltration, or reverse osmosis. When installed, the membrane is sealed by a sealant on its periphery at the opening either on the concentration chamber or on the filtrate chamber, or both.

The membrane is commonly secured on the permeate side, in order to withstand the pressure. An inlet is provided in order to introduce a liquid sample into the concentration chambers and an outlet is provided for the release of the filtrate from the filtrate chamber. In the so-called tangential flow apparatuses, an additional outlet is made in the concentration chamber for the purpose of allowing the circulation of the sample.

It is clear, that the sealant of the membrane must undergo very severe demands, so that the liquid to be treated is prevented from circumventing the membrane. The membrane can be sealed in a multitude of ways. This can be done by heat sealing, sealing with adhesive or solvent, ultrasonic welding or by pressure fit.

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Material and wall thickness of the chambers, which likewise are bound together by sealant, are so selected, that they withstand the pressure of operation.

The apparatuses are, in many cases, additionally provided with separate pressure retaining means or membrane arrangements which are placed between external pressure plates and are typically screwed together, in order to acquire additional holding power.

One of the problems with apparatuses in accord with the state of the technology, is the difficulty of achieving a satisfactory compromise between maintaining low manufacturing costs and, in turn, the reliability of an appropriate pressure retention capacity for the sealing of the membranes and/or for sealing the connection locations between the chambers.

In an effort to achieve a practical design and holding to reasonable costs, it is desirable to connect filtration apparatus by molding. However, it is not always possible to mold membrane layer sections of sufficient thickness, so that they can withstand the high operating costs, since it is difficult, in the molding procedures, to mix thick and thin areas. The alternative, of using separate pressure resistant apparatuses or external pressure plates is at once very expensive as well as being impractical for the smaller apparatuses. Further, dependent on the membranes and construction components being used, appropriate sealing systems are frequently very expensive and/or unreliable when they are used at high pressures.

A further problem presents itself, in obtaining a satisfactorily secure sealing between the chambers, especially in the case of non-compatible or non-sealable materials and in applications where apparatuses with large surfaces must resist the higher total pressures.

The centrifugal filtration apparatus described in the US-A-5,647,990, the teachings

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of which are made part of this document, has the disadvantage of the danger of damaging the relatively fragile membrane, if the retainer housing is pushed onto the concentration chamber, since frictional forces could also push the membrane out of its required position.

The pressure retaining ability and the resistance of the sealing means to physical and chemical attack is further limited by the difficulty of molding a sufficiently thick membrane support plate and the insufficient support, which is provided for the closed surface of the membrane because of the underlying filtrate outlet channels The closed surface in this apparatus directly crosses over these outlet channels in accord with the state of the technology. The problem with the frictional forces and the insufficient sealing support becomes more difficult, if the membrane and sealant is not installed into the concentration chamber in the first place, when the sealing and the assembly could be effected in a single step by means of the pressure on the opening of the chamber which is already available on the periphery of the membrane during installation.

The document GB-A-9819686.8 shows a so-called tangential flow apparatus. The commercial position of this apparatus is limited, because it is necessary to shape the components of the apparatus by machining to a sufficient thickness, because of the difficulty of molding said components so that they can withstand high pressure. Additionally, screwed constructions, which are relatively expensive, are necessary in order to hold together the assembled apparatus when under pressure.

It is the purpose of the invention, to create an apparatus of the above stated constructional type, which is simple to manufacture, while it offers an increased, general reliability.

It is a further purpose, to created a procedure, in accord with which, the membrane

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with the apparatus during its assembly, can be sealingly bound together in a single work step.

It is a further purpose, to create an apparatus, wherein it is possible, to select material for the concentration chamber and filtrate chamber, which are not compatible with each other from the standpoint of thermal or ultrasonic sealing means and/or must be compatible with the currently employed membrane.

It is a further purpose to create an apparatus which has a suppurted seal around the entire periphery of the membrane.

It is yet a further purpose of the invention to create an apparatus, which, for example, can be opened and closed again after the carrying out of the treatment procedure. The said opening and closing of the apparatus is for the examination and/or replacement of the membrane, without damaging the concentration chamber, the filter chamber or the membrane. This feature obviously offers a great deal of flexibility.

The problems in the state of the technology find solution in the manner of design of the apparatus and in the procedure for the manufacture of the apparatus, in accord with the definitions in the attached claims. Further purposes, uses and advantages of the this invention are made clear, with a study of the description, which, in reference to the attached drawings, are a part of the more complete description.

It is a purpose of the present invention, to create an apparatus for the simultaneous filtration of a multiplicity of liquid samples, which apparatus is simple to manufacture, while it still offers an increased reliability.

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Fig. 1 **shows a perspective view of an apparatus of the present invention, which is designed as a tangential flow module,**

Fig. 2 **shows a cross-sectional view of the insert in accord with Fig. 1,**

Fig. 3 **shows a side view of the embodiment in accord with Fig. 1,**

Fig. 4 **shows a top view of the assembled embodiment in accord with Fig. 1,**

Fig. 5 **shows a sectional view of the assembled apparatus in accord with Fig. 4,**

Fig. 6 **shows a top view of the upper, transparent part of the apparatus in accord with Fig. 1,**

Fig. 7 **shows a top view of the lower, transparent part of the insert in accord with Fig. 1.**

Fig. 8 **shows a top view of the upper transparent part of a further embodiment of the insert in accord with Fig. 1,**

Fig. 9 **shows a perspective view of a further embodiment of the invention, which is laid out as a centrifugal filtration apparatus,**

Fig. 10 **shows the assembly of the apparatus in accord with Fig. 9,**

Fig. 11 **shows an assembled apparatus in accord with Fig. 9**

Fig. 12a **shows a sectional view of an assembled apparatus according the Fig. 9**

Fig. 12b **shows a sectional view of an assembled apparatus in accord with Fig. 9, which is provided with a variant of the housing bushing, i.e., a sleeve, or shell,**

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Fig13a
Fig13b **These two figures show two horizontal sectional views through the assembled apparatus in accord with Fig. 12a.,**

Fig. 14 **shows schematically a perspective view of an interconnection of the middle part of the invented apparatus, and**

Fig. 15 **shows a sectional view of an assembled apparatus.**

Fig. 1 shows a perspective view of an apparatus in accord with the present invention, which is laid out as a tangential flow filtration module or cell, which can be employed for example, for the concentration or fractionation of macromolecules in a solution. In a filtration system, a filtration module of this construction would be connected to a pump, which, typically, pulls liquid from a sample reservoir and through the module. The liquid is then, normally, recirculated through a loop which includes said module. The module is connected into this loop by means of an inlet 3 and an outlet 4 for the sample liquid. This inlet and this outlet are, according to the invention, placed on an insert 1. The necessary system pressure is built up by a throttling body, that is, a flow restriction, which is positioned on the outlet 4 of the module.

The insert 1 comprises a concentration chamber and a filtrate chamber, which are separated by a membrane. Fig. 6 shows an example of a concentration chamber 10 in the form of a thin channel for the sample liquid, which said chamber is placed in the upper part 12 of the insert (see Fig. 2) which has an inlet 3 and an outlet 4 which are placed on its end sections.

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This chamber is separated from the filtrate chamber 11, which coacts with it, by means of a membrane. The filtrate chamber 11 is to be found in the lower part 6 of the insert 1. An example of a filtrate chamber is presented in Fig. 7.

Conditioned by the pressure difference between the inflow side and the filtrate side of the membrane, the filtrate permeates through the membrane into the filtrate chamber 11 and is removed through the outlet 5 and collected outside of the module.

Fig. 2 shows a cross-section through an example of an insert in accord with Fig. 1. The under part 6 has a generally flat upper surface, i.e., surface 16 which serves as a seat for the membrane 11 or a support therefor. This surface is provided with a plurality of parallel grooves which form the channels 9 for the filtrate, see Fig. 7. These channels all stand in connection with one another, for instance, by means of a collection channel 8 and a transversely running outlet channel 14 as seen in Fig. 5. The transverse outlet channel

14 connects together the end sections of the channel 9 at one side of the insert 1, in order to conduct the total collected filtrate to a filter outlet 5 from which it leaves the module.

The membrane 15, regarding which, see Fig. 5, is on the upper side of the surface 16 and extends along the edge of this upper side to the vertical wall section 13. Along the inside of the said vertical end section 13, on the upper surface 16 is to be found, in this embodiment, a generally flat sealing seat (refer to Figs. 2, 5, 7). This has the meaning, that the membrane, over its entire periphery, has the support of a generally flat seat. A sealing means 7 in the form of an O-ring is placed, in this embodiment, on the upper side of the membrane and over the sealing seat and the upper part 12, which closes the insert.

A housing, (or a shell) 2, 2' is advantageously made by the molding of an appropriate plastic material envelopes the insert. In presented form in the Figs. 1, 3, 4, 5, the

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housing construction is carried out in two parts, namely 2 and 2', which, upon the assembly are pushed together from two opposite directions, thus encasing the insert and forming the complete housing. In the described assembly, the housing presses the insert 1, without frictional force, on the membrane, whereby, simultaneously and in one step, the concentration chamber and the filtrate chamber is created by the sealing of the peripheral edges of the membrane.

In this way, by means of a simple assembly of a definite number of separate components, without recourse to tools or adhesives, it becomes possible to realize a filtration module, for which formerly, adhesives, screwed pressure plates, assembly tools and the like were necessary.

Additionally this module without any further steps, can be disassembled for examination, for change of membrane, for cleaning or for any other purpose, without damaging the components.

Fig 3 shows a side view of the embodiment in accord with Fig. 1. The introduction of the insert into the two housing parts proves to be very easy, due to the wedge form and tapering of the housing and the insert, in his respect, see Fig. 5. A greater force is necessary only during the compression of the sealing means at the end of the assembly.

It would even be possible to employ shrink-fit technology to bring the housing into position.

Fig. 4 shows a top view of the embodiment in accord with Fig. 1 in the assembled condition. On the lower part of the housing, in this embodiment, is placed a dovetailed edge or flange 17, which can coact with a corresponding slot or groove on the upper part of a neighboring module (not shown). In this manner, filtration modules can be stacked, one on the other, in accord with the necessities of the application.

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Fig. 5 shows a cross-section of the assembled apparatus shown in Fig. 4. As may be easily seen, the interior of the molded housing is designed in a wedge shape, i.e., tapeed. This is obviously practical for manufacturing purposes, but also creates the possibility of achieving the necessary compression force for the insert 1, if this likewise exhibits a wedge shape. In order to gain practically the same compression effect, however, with a lesser friction between the housing and the insert during assembly, the upper and lower surfaces of the insert could be made to be parallel and the wedge shape could be effected by means of sloped edges or flanges running in the longitudinal direction and placed on the upper and lower surfaces, or, at least on one of the two. Such a design is presented in Fig. 8, wherein the wedge shaped edge or flange is denoted by the number 18.

An additional advantage of the molded housing being in two parts, 2, 2' in accord with the foregoing embodiments, is to be found therein, in that a standard threading for the inlet 3 and the outlet 4 for the sample liquid can be made without any further steps during the process of molding.

There are many variants at hand of the invented idea. For instance, it could be of advantage, in certain embodiments to place the sealing means between the membrane and the filtrate chamber. It is plain to be seen, that a great flexibility in regard to the selection of materials for the various components of the filtration module stands available. A connection or adhesion material compatibility between any of the components of this embodiment is not necessary.

This means that, for instance, a relatively soft and flexible material can be used for

the insert, or for part thereof, while for the housing a relatively rigid, stiff and resistant material can be employed. In this way, the sealing means can be integrated in the upper

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and/or the lower part 6, 12 of the insert. The sealing means could assume the form of a border, an edging, or a groove around the periphery of the upper an/or lower parts and be of the same material as the said lower and upper parts 6, and 12 respectively.

The chemical characteristics of the different components can again be chosen with the greatest flexibility. A material with a high resistance to solvents could, for example, be chosen for the inner construction, which would be wet in the course of the flow of the liquid.

The two housing parts, 2, 2' are shown with closed end sections. This construction provides a very firm and rigid housing, which can resist very high pressures. Obviously, these end pieces are not necessarily required for all applications.

Fig. 9 shows a perspective view of a further embodiment of the apparatus in accord with the invention, wherein the apparatus is constructed in the form of a centrifugal filtration apparatus. Components, which represent the parts related to the embodiments described in accord with Figs. 1 to 8, are designated by the same reference numbers. In this way, a concentration chamber 10 is provided, in order to accept the sample to be treated. In this case, the sample is not recirculated into this chamber, and hence, no outlet from the chamber is provided for the sample, but only the inlet 3. A sealing means 7 is so installed, that it is to be found in a groove 19, i.e. a recess around an opening in the wall of the chamber. An appropriate membrane piece 15 is placed over the opening. In the same manner as previously described, a filtrate chamber is created by means of lower part 6, when it is fastened against the membrane 15, which chamber is provided with a membrane supporting, seat area plus a plurality of vertical, parallel grooves, which grooves form channels 9 for the filtrate.

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Fig. 10 shows the assembled components 12, 7, 15 and 6 of the centrifugal apparatus in accord with Fig. 9. A one-piece housing 2", in this embodiment, slidingly

encapsulates the assembled components. Because of the wedge or conical shape of the component "lower part" 6, i.e. the filtrate chamber, and the corresponding inner shape of the housing, the filtrate chamber is pressed against the membrane 15, which in turn presses the sealing arrangement against the concentration chamber. It is to be noted, that the membrane is subjected only to forces perpendicular to its surface or area, when the housing is put into position.

In this manner, a pressure is created and maintained during the centrifuging process. This pressure is sufficiently high to seal off the membrane fluid-tightly against the concentration chamber.

Fig. 11 shows the assembled apparatus with the housing in its position.

Fig. 12a shows a cross-section of an assembled apparatus in accord with Fig. 9. On the upper part of the filtrate chamber, is to be found a ventilation or air release channel 20 which connects with the ambient atmosphere. This channel can evacuate air from the filtrate channels 9 at the start of the filtration process. In this embodiment are provided three channels 5' for the outlet of the filtrate, which is collected in a (not shown) filtrate tube, into which the apparatus is partially set during the process. The channels 5' connect, as is the case in the embodiment shown in Fig. 5, on the inside with a transversely running outlet channel 14. This outlet channel 14 connects in turn with the end section of the channel 9 on one side of the filtrate chamber, in order that the entire, collected filtrate is conducted to the outlet channels 5'.

With flange 21, the apparatus seats itself on the housing 2, specifically on the rim of the filtrate tube, which means, that the centrifugal forces acting upon the apparatus during

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the process hold the housing firmly in its position with the flange 22 of the upper part against the flange 21 of the lower part.

Fig. 12b shows a cross-section of an assembled apparatus in accord with Fig. 9, which is provided with a variant of the housing. In order to secure the sealing means between sealing ring 7 and the membrane on the lower part, the housing in this area is made less flexible, since a stabilization ring 23 of material around the opening is added in

its lower part. The ring 23 can be, alternately, of a flatter configuration than that shown in cross-section in figure 12b.

So that the vertical filtrate channels 9 in this and other embodiments do not extend under the transversely running outlet channel 14, it is possible to create a generally flat seating support for the permeate side of the membrane 15 along its periphery, which assures a uniform sealing action throughout the entire periphery.

Fig. 13a shows a horizontal cross-section through the assembled apparatus, in accord with Fig. 12a in the upper part, and Fig. 13b depicts a cross-section through the lower part. The wedge shape, that is the intake slope, of the component 6, which forms the filtrate chamber, is clearly presented.

It is clear, the many variation of the fundamental invented concept can be presented. In this way, could first be shown invented apparatuses designed especially for use in a centrifuge, such as were described in relation to the embodiment shown in Figs. 9 through 13.

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Gas pressure or liquid pressure or yet vacuum may be employed, in order to create the vector, i.e. the gradients in order to drive the solvent and the small molecules through the membrane, or, on the other hand, to pull them through. The first embodiment in accord with the foregoing types of construction employs, for example, liquid pressure.

The apparatus for sealing can take the form of an O-ring, which advantageously be positioned into a corresponding groove about one of the two openings. Also two O-rings can be considered, whereby, one is present around each opening. As already mentioned, in relation to the foregoing descriptions of the first embodiment, the sealing means of the membrane can be achieved by a seal, which is integrated into one or both chambers. This mode of construction is of advantage, when softer material is used for f the chambers or for parts thereof. Generally, the flexibility in regard to the selection of material for the various components (mechanical properties, chemical characteristics, etc.), which were first mentioned in the above first embodiment, remain valid for all embodiments.

The apparatus, in accord with the invention, for the simultaneous filtration of a multiplicity of liquid samples (Figs. 14, 15) comprises an insert 1 which is composed of a two part housing 2, 2', enclosing this insert 1. The insert 1 is made up of a component 6, which is designed as a support plate, a sealing means in the form of a seal mat 7, flat filtering means, i.e. membranes 15 and a plate 27 with a multiplicity of concentration chambers 10. The component 6 includes a plurality of openings 24, which, advantageously, in their number and arrangement correspond to the number and arrangement of the receptacles 25 of a micro titer plate 26. The openings 24 of the component 6 can be additionally equipped with a filter support, which in turn possesses the collection channel 8 and conduits for the outlet of filtrate 5'. A favorably elastic seal mat 7 is laid upon the component 6 and has through openings 28 aligned to coincide with openings 24, which correspond to the number of the openings 24 of the component 6 serving as a support plate. Advantageously, for the easier positioning of the sealing mat 7 on the component 6 and for a more secure sealing of the filtering means, i.e. the membrane 15, against the filtrate chambers 11, partitions or webs 29 are installed surrounding the openings 24 of the component 6.

On that side of the sealant/sealing mat 7, which is remote from the component 6, this serving as a support plate, the through openings 28 are encircled by collars 30. The collars 30, have a larger inner width than the width of the through openings 28, sized in such a way, that on the base in the interior of the collars 30 a surrounding flange 31 is constructed out of the sealant material. During the assembly, the flat filtering means, i.e. membranes 15 are laid on the circumferentially running flange 31 of the collars 30. Within the collars 30, during assembly of the apparatus, the chambers 10 are inserted, for instance, in the form of small tubes, which are open on both ends and are connected to the plate 27. The chambers 10, possess outer circumferential surfaces, which are congruent with the inner surfaces of the collars 30. The chambers 10 serve, first, for the reception of the liquid samples. Second, the chambers function in coaction with the sealing apparatus 4 of the liquid tight rim seal of the flat filter means, i.e. membranes 15 between the

encircling flange surface 31 in the interior of the collars 30 and the lower, open end of the chambers 10. The collars 30 are pushed so far into the chambers 10, that their under ends pressingly lie against the edge area of the filtering means, i.e. membranes. The two-part housing 2, 2', is provided with inlet openings 3 on the upper side for the liquid samples. On the underside, the housing 2, 2' has outlet openings 5 for the filtrate, which outlet openings are congruent to the openings 24 of the component 6. During the putting together of the apparatus, the two housing parts 2, 2', are pushed over the combined insert 1 in such a manner, that the housing 2" is closed. As this is done, such compression forces are so created and made permanent, that they are of sufficient magnitude to hold the filtering means, i.e. membranes 15 liquid tight against the flanges 31 of the collars 30. For this purpose, the insert 1 possesses a conical outer profile, and the housing 2" has a conical inner profile, which, upon fitting together, work in common to create the compressive forces. As is shown in the Fig. 14, the component 6, serving as a support plate, and the plate 27 are equipped with lateral, wedge shaped flanges 18. When the housing is closed, the inlet openings 3 align on the upper side of the housing 2", the ends of the chamber 10, i.e. the through chamber 10 to the sealing mat 28, the opening 24 of the support plate 6 and the outlets 5' of the underside of the housing 2", all lie in a straight line. As may be seen from Fig. 15, the outlets 5 on the underside of the housing 2" are equipped with filtrate outflow fittings 32, by means of which, the apparatus is placed as a filter assembly upon a micro titer plate 26.

A procedure for the manufacture of the apparatus, in accord with the invention, encompasses the following steps:

A sealing means is first placed about at least one of the openings in the concentration chamber or in the filtrate chamber. One of the openings is subsequently covered with a membrane, whereby the feed side of said membrane lies in the concentration chamber and the permeate side of said membrane lies in the filtrate chamber, that is, the two chambers are on opposite sides of said membrane. The chambers are subsequently assembled, whereby the openings are placed one above the other, and a pressure resistant housing,

also known as a sleeve, or a shell, is next placed outside and encapsulating the combined assembly of the concentration chamber, the sealing arrangement, the membrane and the filtrate chamber. The housing creates a pressure, which is sufficiently great, to make the membrane liquid-tight during the process against at least one of the chambers and to maintain this said pressure while the structural strength, the rigidity and the carrying capacity of the construction of the entire apparatus is increased.

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Reference Numbers and Equipment Items

1	Insert
2, 2'	Parts of two part housing
2"	One part housing
3	Inlet fitting
4	Outlet fitting
5	Outlet fitting
5'	Channel for outlet
6	Lower part (see Fig. 5), a component (see Figs. 9, 14, 15)
7	Seal (O-ring type and matting)
8	Collection channel
9	Channel
10	Concentration chamber
11	Filtrate chamber
12	Upper part
13	Vertical wall section
14	Outlet channel
15	Membrane
16	Surface
17	Dovetailed flange, for edge
18	Flange

19	Groove
20	Ventilating and air release fitting
21	Flange
22	Flange
23	Stabilizing ring
24	Openings
25	Depressions, or receptacle openings of a micro titer plate
26	Micro titer plate (see attached illustration)
27	Plate
28	Through opening, a perforation,
29	Collar or web (for separating receptacles)
30	Collar (reinforcing concentration chamber tube)
31	Circumferential (or peripheral) flange
32	Filtrate outlet (pipe, tube) fitting

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Claims

Claimed is:

1. An apparatus for the concentration and/or purification of macromolecules in a solution by means of filtration through a membrane (15), comprising a concentration chamber (10) for a liquid sample to be treated, which is provided with a first opening, a filtrate chamber (11), which is provided with a second opening, which is to be placed above the first opening, a membrane (15), which is installed fluid-tight along its periphery and which divides the two stated chambers, therein characterized, **in that** a sealing arrangement (7) is placed about at least one of the openings in contact with at least one side of the membrane (15), and **in that** the filtrate chamber, on the side facing the membrane (15) or on the side lying opposite to this, is provided with a membrane support, that is a membrane seat, which supports the filtrate side of the membrane, and **in that** a pressure resistant housing (2, 2', 2") encapsulates the assembly of the concentration chamber (10), the sealing arrangement (7), the membrane (15) and the filtrate chamber (11) on the outside so that thereby, the arrangement is complete and during the assembly process compression forces are generated and maintained which are sufficiently great to seal the membranes fluid-tight against at least one of the chambers (10, 11), while also the structural strength and load capacity of the structure of the entire arrangement is increased.

2. An apparatus in accord with Claim 1, therein characterized, in that the sealing means (7) has the form of a ring shaped, elastic seal of the O-ring type.

3. An apparatus in accord with Claim 1, therein characterized, in that the sealing means (7) has the form of a grating of elastic material and forms an integral component of at least one of the chambers.

4. An apparatus in accord with one of the Claims 1 to 3, therein characterized, **in that** the housing (2") is ring shaped and has a tapering or inclined inner surface and **in that** at least one of the chambers (10, 11) has a tapering or inclined outer surface, which surfaces in coaction during assembly generate compression forces.

5. An apparatus in accord with one of the Claims 1 to 4, therein characterized, in that a multiplicity of concentration chambers (10) exists for the simultaneous filtration of a plurality of liquid samples, and the insert (1) is formed:

- from a component (6) which serves as a support plate with a plurality of openings (24),
- from the sealing apparatus (7) laid on the component (6) in the form of a sealing mat with through-passages (28) aligned with the said openings (24) of the component 6, and
- with collars (30) on that side of the sealing mat which is proximal to the component (6), which collars (30) enclose the said through-passages (28) of the sealing mat, these said collars being if a greater inner width that the width of the through-passages (28) to the extent that, on the basis in the interior of the collars (30) a peripheral bearing seat (31) is formed
- from individual flat membranes (15), which lie on the circumferentially running seat surfaces (31) of the collars (30), from a plate (27) with a plurality of parallel, chambers (10) open at both ends to receive the liquid samples with outer peripheral surfaces, which are congruent to the inner peripheral surfaces of the collars (30)
- whereby the chambers (10) are so far thrust into the said collars (30), that their under ends lie on the membranes (15) and
- whereby the two part housing (2, 2') is provided a multitude of inlets (3) for the liquid samples and on the underside is provided with a multitude of outlets (5) for filtrate, which are congruent to the openings (24) of the component (6) serving as a support plate,
- whereby the two housing parts (2, 2') are thrust over the inset (1) in such a manner that the housing (2") is closed, and whereupon compression forces were created and upheld, which pressures were sufficiently high in order that

the membranes (15) are made fluid-tight against the seat surfaces 31 of the collars (13) to seal off and

- whereby in the closed housing condition the inlets (3) of the upper side of the housing (2") the ends of the chambers (10), the through penetrations (28), the sealing arrangement (7), the openings (24) of the component (6) and the outlets (5) on the under side of the housing (2") lie in alignment along a straight line.

6. An apparatus in accord with Claim 5, therein characterized, in that the openings (24) of the component (6) are furnished with filtrate outlet fittings (32).

7. A procedure for the manufacture of an apparatus for the concentration and/or purification of macromolecules in a solution by means of filtration through a membrane (15), wherein the apparatus is provided with a concentration chamber (10) for a liquid sample to be treated, said chamber having a first opening, and provided with a filtrate chamber (11) having a second opening, with a membrane 15 extending over one of the first or second openings and along their peripheral outlines in a fluid-tight manner whereby said membrane (15) separates the two chambers (10, 11), therein characterized, in that the said procedure possesses the following steps:
   - a sealing arrangement (7) is placed on at least one of the openings,
   - one of the openings is covered with a membrane (15) whereby its feed side serves for the concentration chamber (10) and the filtrate side serves for the filtrate chamber (11)
   - the chambers (10, 11) are assembled, wherein the first opening is placed over the second opening, and
   - a pressure resistant housing (2, 2' 2") is placed on the outside and encapsulates the assembly of the concentration chamber (10), the sealing arrangement (7), the membrane (7) and the filtrate chamber (11), so that, thereby the arrangement if made complete and during the process pressure forces are created and maintained, and are of sufficient intensity to seal off the membrane (15) fluid-tight against at least one of the chambers (10, 11), while, at the same time, the structure of the entire arrangement is increased.

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